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EXAMINER	
BLANCHARD, DAVID J	

ART UNIT	PAPER NUMBER
1642	

DATE MAILED: 08/17/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/005,480	CHALLITA-EID ET AL.	
	Examiner	Art Unit	
	David J Blanchard	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *6/21/2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *4-7,9-15,65-70 and 75-89* is/are pending in the application.

4a) Of the above claim(s) *11, 14, 15, 65-70, 75-77 and 84-89* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *4-7,9,10,12,13 and 78-83* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *5/21/03; 5/10/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Claims 4-7, 9-15, 65-70 and 75-89 are pending.

Claims 4, 12, 14-15, 65-68, 70, 75, 81 and 87 have been amended.

Claims 1-3, 8, 16-64 and 71-74 have been canceled.

2. Applicant's election without traverse of Group I, claims 4-7, 9-10, 12-13 and 78-83 in the reply filed on 6/21/2004 is acknowledged.

3. Claims 11, 14-15, 65-70, 75-77 and 84-89 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention.

4. Claims 4-7, 9-10, 12-13 and 78-83 are under examination.

Specification

5. The disclosure is objected to because of the following informalities:

a. The disclosure is objected to because it contains embedded hyperlinks and/or other form of browser-executable code. For example, see page 22, line 35, page 25, lines 27-30, page 26, line 14 and pages 44 and 105. Applicant is required to check the entire disclosure and delete all the embedded hyperlinks and/or other form of browser-executable code. See MPEP § 608.01.

b. The lengthy specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is

requested in correcting any errors of which applicant may become aware in the specification.

Appropriate correction is required.

Claim Rejections - 35 USC § 101

6. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claim 4 is rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. Claim 4, as written, does not sufficiently distinguish an antibody that binds SEQ ID NO:743 as it exists naturally because the claims do not particularly point out any non-naturally occurring differences between the claimed antibody and the naturally occurring antibody. The claimed antibodies (not antigen binding fragments) read upon antibodies as they are naturally synthesized in eukaryotic cells.

In the absence of the hand of man, the naturally occurring antibodies are considered non-statutory subject matter (Diamond v. Chakrabarty, 206 U.S.P.Q. 193 (1980)). It should be noted that the mere purity of a naturally occurring product does not necessarily impart patentability (Ex parte Siddiqui, 156 U.S.P.Q. 426 (1996)). However, when purification results in a new utility, patentability is considered (Merck Co. v. Chase Chemical Co., 273 F. Supp 68 (1967), 155 U.S.P.Q. 139, (District Court,

New Jersey, 1967)). The claims should be amended to indicate the hand of the inventor, e.g., by insertion of "Isolated" or "Purified". See MPEP 2105.

Claim Rejections - 35 USC § 112

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claims 4-7, 9-10, 12-13 and 78-83 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

The claims are drawn to an antibody and a hybridoma that produces said antibody that binds to a protein at least 90% homologous to SEQ ID NO:743. The specification discloses only the human 161P2F10B polypeptide (SEQ ID NO:743). The specification discloses that naturally occurring allelic variants share at least 90% homology with human 161P2F10B (i.e., SEQ ID NO:743) (see page 23). The specification does not disclose any polypeptide that is at least 90% homologous to SEQ ID NO:743 except SEQ ID NO:743.

The general knowledge in the art concerning homologous proteins does not provide any indication of how the structure of one homolog is representative of unknown homologs. Reiger et al. (Glossary of Genetics and Cytogenetics, Classical and

Molecular, 4th Ed., Springer-Verlay, Berlin, 1976) clearly define alleles as one of two or more alternative forms of a gene occupying the same locus on a particular chromosome... and differing from other alleles of that locus at one or more mutational sites (page 17). Thus, the structure of naturally occurring allelic sequences that would be at least 90% homologous to the protein of SEQ ID NO:743 are not defined. With the exception of SEQ ID NO:743 the skilled artisan cannot envision the detailed structure of the encompassed homologous proteins and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Thus, one of skill in the art would not understand that the applicant had possession of the claimed invention at the time the instant application was filed.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116). As discussed above, the skilled artisan cannot envision the detailed chemical structure of the encompassed genus of polypeptides, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The

compound itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

One cannot describe what one has not conceived. See *Fiddles v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddles*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

Therefore, only the protein comprising the sequence set forth in SEQ ID NO:743, but not the full breadth of the claim meets the written description provision of 35 U.S.C. §112, first paragraph. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

9. Claims 4-7, 9-10, 12-13 and 78-83 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an antibody and a hybridoma that produces and antibody that binds a protein comprising SEQ ID NO:743, does not reasonably provide enablement for an antibody or a hybridoma that produces an antibody that binds to a protein at least 90% homologous to SEQ ID NO:743. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The factors considered when determining if the disclosure satisfies the enablement requirement and whether any necessary experimentation is undue include,

but are not limited to: 1) nature of the invention, 2) state of the prior art, 3) relative skill of those in the art, 4) level of predictability in the art, 5) existence of working examples, 6) breadth of claims, 7) amount of direction or guidance by the inventor, and 8) quantity of experimentation needed to make or use the invention. *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

The claims are drawn to an antibody and a hybridoma producing an antibody that binds a protein at least 90% homologous to SEQ ID NO:743. The specification teaches the polypeptide of SEQ ID NO:743 (i.e., 161P2F10B), which is identical to the ENPP3 phosphodiesterase I ecto-enzyme (also called CD203c or PD-1 beta) belonging to a family of ectonucleotide phosphodiesterases and pyrophospahatases (see page 107). The specification teaches that the ENPP enzymes are involved in extracellular nucleotide metabolism, nucleotide signaling, and recycling of extracellular nucleotides as well as cell-cell and cell-matrix interactions (see page 107). The specification also teaches that 161P2F10B (SEQ ID NO:743) is useful as a diagnostic and therapeutic target for kidney and prostate cancers, metastatic cancers and other human cancers that express this protein (see Examples 39-40 at pages 108-110). However, the specification teaches that ENPP enzymes differ in their substrate specificity and tissue distribution (see page 107, line 35). Thus, one would not know if the protein with the claimed homology would function as a protein of SEQ ID NO:743. The specification has not taught any protein that is at least 90% homologous to SEQ ID NO:743 (161P2F10B) or any antibody that binds to such protein or the use of such antibody.

The specification does not teach how to make or use the claimed variant proteins, which are defined by the specification as allelic variants, homologs, analogs as well as variants that include conservative substitutions (see page 23). This does not provide sufficient, specific guidance, enabling the skilled artisan to make and/or use the invention without undue experimentation. The specification does not disclose the extremely large number of proteins broadly encompassed by the claims and the claims broadly encompass a significant number of inoperative species.

While recombinant and mutagenesis techniques are known, it is not routine in the art to screen for multiple substitutions or multiple modifications of other types and the positions within the protein's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining similar biological activity are limited in any protein. The result of such modifications is unpredictable based on the instant disclosure. One skilled in the art would expect any tolerance to modification shown for a given protein to diminish with each further and additional modification, e.g., multiple substitutions. The sequence of some proteins is highly conserved and one skilled in the art would not expect tolerance to any amino acids modifications in such proteins. The specification does not support the broad scope of the claims, which encompass all modifications and fragments because the specification does not disclose the following:

a. The general tolerance to modification and extent of such tolerance;

b. The specific positions and regions of the sequence which can be predictably modified and which regions are critical;

c. What fragments, if any, can be made which retain the biological activity of the intact protein; and

d. The specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Thus, applicant has not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed protein in a manner reasonably correlated with the scope of the claims broadly including any number of additions, deletions, or substitutions and fragments of any size. The scope of the claims must bear a reasonable correlation with the scope of enablement. See In re Fisher, 166 USPQ 19 24 (CCPA 1970). Without such guidance, the changes which can be made in the protein's structure and still maintain biological activity is unpredictable and the experimentation left to those skilled in the art is unnecessarily and improperly extensive and undue. See Amgen, Inc. v. Chugai Pharmaceutical Co. Ltd., 927 F,2d 1200, 18 USPQ 1016 (Fed. Cir. 1991) at 18 USPQ 1026 1027 and Ex parte Forman, 230 USPQ 546 (BPAI 1986).f.

Furthermore, protein chemistry is probably one of the most unpredictable areas of biotechnology. For example, the replacement of a single lysine at position 118 of the acidic fibroblast growth factor by a glutamic acid led to a substantial loss of heparin binding, receptor binding, and biological activity of the protein (see Burgess et al, Journal of Cell Biology Vol 111 November 1990 2129-2138). In transforming growth factor alpha, replacement of aspartic acid at position 47 with asparagine, did not affect biological activity while the replacement with serine or glutamic acid sharply reduced the

biological activity of the mitogen (see Lazar et al Molecular and Cellular Biology Mar 1988 Vol 8 No 3 1247-1252). Replacement of the histidine at position 10 of the B-chain of human insulin with aspartic acid converts the molecule into a superagonist with 5 times the activity of nature human insulin. Schwartz et al, Proc Natl Acad Sci USA Vol 84:6408-6411 (1987).

Lederman et al (Molecular Immunology 28:1171-1181, 1991) disclose that a single amino acid substitution in a common allele ablates binding of a monoclonal antibody (see entire document).

Li et al (Proc. Natl. Acad. Sci. USA 77:3211-3214, 1980) disclose that dissociation of immunoreactivity from other activities when constructing analogs (see entire document).

Coleman P. M. (Research in Immunology, 145:33-36, 1994) discloses that even single amino acid changes within the interface of an antibody-antigen complex can alter the interaction by driving the affinity towards more tightly bound complexes or effectively abolish the interaction entirely (see page 33).

Although biotechnology has made great strides in the recent past, these references serve to demonstrate exactly how little we really know about the art. The art of protein chemistry remains very unpredictable as Burgess et al, Lazar et al, Schwartz et al, Lederman et al, Li et al and Coleman P. M. conclusively demonstrate.

In view of the lack of guidance, lack of examples, and lack of predictability associated with regard to producing and using the myriad of homologous proteins (i.e., 90% homologous to SEQ ID NO:743) as well as antibodies that bind such proteins as

encompassed by the scope of the claims, one skilled in the art would be forced into undue experimentation in order to practice the broadly claimed invention.

Claim Rejections - 35 USC § 102

10. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

11. Claims 4-7 and 78-79 are rejected under 35 U.S.C. 102(a) as being anticipated by Buhring et al [a] (Blood 97(10):3303-3305, 15 May 2001) as evidenced by Hua et al (Genomics 45(2):412-415, 1997).

Claims 4-7 and 78-79 are drawn to a monoclonal antibody that binds to a protein that is at least 90% homologous to SEQ ID NO:743, wherein the antibody is labeled with a detectable label, or a diagnostic agent and the antibody is recombinantly produced.

Buhring et al [a] teach monoclonal antibody 97A6 that binds E-NPP3 (ectonucleotide pyrophosphatase phosphodiesterase-3) also known as PDNP3 or PD-

1β (phosphodiesterase I/nucleotide pyrophosphatase-3), which is identical to the protein of SEQ ID NO:743 as evidenced by Hua et al (see Figure 1 and the alignment attached to the back of this office action) (see entire document, particularly page 3303, left column). Hua et al evidence that the sequence of PDNP3 is identical to the instantly claimed protein of SEQ ID NO:743. Thus, as a property is inherent to a product, the monoclonal antibody 97A6 would bind the protein of SEQ ID NO:743. Buhring et al [a] teach monoclonal antibody 97A6 labeled with phycoerythrin, which is an agent, a detectable marker and a diagnostic agent (see page 3303, right column). Claim 6 is drafted in the product-by-process format. The reference does not describe the production of the molecule using the methods identical to that is recited in claim 6. However, the recitation of a process limitation in claim 6 is not viewed as positively limiting the claimed product absent a showing that the process of making recited in claim 6 imparts a novel or unexpected property to the claimed product, as it is assumed that equivalent products are obtainable by multiple routes. The burden is placed upon the applicants to establish a patentable distinction between the claimed and reference products. The method in which the antibodies that bind the protein of SEQ ID NO:743 were produced is immaterial to their patentability. Even though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process. *In re* Thorpe, 227 USPQ 964, 966 (Fed. Cir. 1985). See

also MPEP 2113.

12. Claims 4-7, 12 and 78-79 are rejected under 35 U.S.C. 102(b) as being anticipated by Buhring et al [b] (Blood 94(7):2343-2356, 1 October 1999) as evidenced by Buhring et al [a] (Blood 97(10):3303-3305, 15 May 2001) and as evidenced by Hua et al (Genomics 45(2):412-415, 1997).

Claims 4-7, 12 and 78-79 have been described supra.

Claim 12 is drawn to a hybridoma that produces a monoclonal antibody that binds to a protein at least 90% homologous to SEQ ID NO:743.

Buhring et al [b] teach monoclonal antibody 97A6 (see entire document) and as evidenced by Buhring et al [a] monoclonal antibody 97A6 specifically binds E-NPP3 (ectonucleotide pyrophosphatase phosphodiesterase-3) also known as PDNP3 or PD-1β (phosphodiesterase I/nucleotide pyrophosphatase-3), which is identical to the protein of SEQ ID NO:743 as evidenced by Hua et al (see the alignment attached to the back of this office action). Buhring et al [a] evidence that monoclonal antibody 97A6 specifically binds PDNP3 (see page 3303, left column) and as evidenced by Hua et al the sequence of PDNP3 (see Figure 1) is identical to the instantly claimed protein of SEQ ID NO:743. Thus, as a property is inherent to a product, the monoclonal antibody 97A6 would bind the protein of SEQ ID NO:743. Buhring et al [b] teach a hybridoma producing monoclonal antibody 97A6 and the 97A6 antibody is labeled with phycoerythrin, which is an agent, a detectable marker and a diagnostic agent (see page 2344, left column). Claim 6 is drafted in the product-by-process format. The reference does not describe

the production of the molecule using the methods identical to that is recited in claim 6. However, the recitation of a process limitation in claim 6 is not viewed as positively limiting the claimed product absent a showing that the process of making recited in claim 6 imparts a novel or unexpected property to the claimed product, as it is assumed that equivalent products are obtainable by multiple routes. The burden is placed upon the applicants to establish a patentable distinction between the claimed and reference products. The method in which the antibodies that bind the protein of SEQ ID NO:743 were produced is immaterial to their patentability. Even though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process. *In re* Thorpe, 227 USPQ 964, 966 (Fed. Cir. 1985). See also MPEP 2113.

13. Claims 4-7, 12 and 78-79 are rejected under 35 U.S.C. 102(e) as being anticipated by Buhring H-J [c] (U.S. Patent 6,323,321 B1, filed 6/30/1999) as evidenced by Buhring et al [a] (Blood 97(10):3303-3305, 15 May 2001) and as evidenced by Hua et al (Genomics 45(2):412-415, 1997).

The claims have been described supra.

Buhring H-J [c] teach monoclonal antibody 97A6 (see entire document) and as evidenced by Buhring et al [a] monoclonal antibody 97A6 specifically binds E-NPP3

(ectonucleotide pyrophosphatase phosphodiesterase-3) also known as PDNP3 or PD-1β (phosphodiesterase I/nucleotide pyrophosphatase-3), which is identical to the protein of SEQ ID NO:743 as evidenced by Hua et al (see the alignment attached to the back of this office action). Buhring et al [a] evidence that monoclonal antibody specifically binds PDNP3 (see page 3303, left column) and as evidenced by Hua et al teach the sequence of PDNP3 (see Figure 1) is identical to the instantly claimed protein of SEQ ID NO:743. As a property is inherent to a product, the monoclonal antibody 97A6 would bind the protein of SEQ ID NO:743. Buhring H-J [c] teach a hybridoma producing monoclonal antibody 97A6 and the 97A6 antibody is labeled with phycoerythrin, which is an agent, a detectable marker and a diagnostic agent (see page 2344, left column). Claim 6 is drafted in the product-by-process format. The reference does not describe the production of the molecule using the methods identical to that is recited in claim 6. However, the recitation of a process limitation in claim 6 is not viewed as positively limiting the claimed product absent a showing that the process of making recited in claim 6 imparts a novel or unexpected property to the claimed product, as it is assumed that equivalent products are obtainable by multiple routes. The burden is placed upon the applicants to establish a patentable distinction between the claimed and reference products. The method in which the antibodies that bind the protein of SEQ ID NO:743 were produced is immaterial to their patentability. Even though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same or obvious from a

product of the prior art, the claim is unpatentable even though the prior product was made by a different process. *In re* Thorpe, 227 USPQ 964, 966 (Fed. Cir. 1985). See also MPEP 2113.

Claim Rejections - 35 USC § 103

14. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to

consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

15. Claims 4-7, 9-10, 13 and 78-83 are rejected under 35 U.S.C. 103(a) as being unpatentable over Buhring et al [a] (Blood 97(10):3303-3305, 15 May 2001) as evidenced by Hua et al (Genomics 45(2):412-415, 1997) in view of Thorpe et al (U.S. Patent 6,342,219 B1, filed 4/28/2000).

The claims have been described supra.

Claims 9-10 and 13 further limit the antibody that binds to a protein at least 90% homologous to SEQ ID NO:743 by reciting wherein the antibody is selected from a Fab, F(ab)2, Fv, scFv (interpretation of sFv), a human, a humanized or a chimeric antibody. Claims 80-83 further limit the labeled antibody that binds to a protein at least 90% homologous to SEQ ID NO:743 by reciting various cytotoxic agents, radioactive isotopes, chemotherapeutic agents and toxins as agents for labeling the antibody.

Buhring et al [a] as evidenced by Hua et al have been described supra. Buhring et al [a] does not specifically teach a Fab, F(ab)2, Fv, scFv (interpretation of sFv), a human, a humanized or a chimeric antibody or cytotoxic agents, radioactive isotopes, chemotherapeutic agents and toxins as agents for labeling the antibody. These deficiencies are made up for in the teachings of Thorpe et al.

Thorpe et al teach teach immunoconjugates and immunotoxins for tumor therapy, wherein the antibody is a Fab, Fv, single-chain Fv, a human or humanized antibody (see columns 72-73 and 14). Thorpe et al teach that the antibody is coupled to toxins that are plant, fungus, or bacterial derived toxins (see column 29, lines 1-18) or

coupled to radioactive isotopes (see column 39, lines 31-44) or coupled to chemotherapeutic agents including taxol, vinblastine, vincristine, colchicines as well as others (see column 29, lines 38-43).

It would have been prima facie obvious to one of ordinary skill in the art at the time the claimed invention was made to have coupled the therapeutic and diagnostic agents taught by Thorpe et al to the 97A6 monoclonal antibody as taught by Buhring et al [a] for tumor therapy.

One of ordinary skill in the art would have been motivated to and had a reasonable expectation of success at the time the invention was made to have coupled the therapeutic and diagnostic agents taught by Thorpe et al to the 97A6 monoclonal antibody as taught by Buhring et al [a] for tumor therapy because Buhring et al [a] teach labeled monoclonal antibody 97A6 that binds E-NPP3 also known as PDNP3 or PD-1β, which is identical to the protein of SEQ ID NO:743 as evidenced by Hua et al (see the alignment attached to the back of this office action) and Thorpe et al teach immunoconjugates and immunotoxins for tumor therapy, wherein the antibody is a Fab, Fv, single-chain Fv, a human or humanized antibody and the antibody is coupled to toxins that are plant, fungus, or bacterial derived toxins (see column 29, lines 1-18) or coupled to radioactive isotopes (see column 39, lines 31-44) or coupled to chemotherapeutic agents such as taxol, vinblastine, vincristine, colchicines as well as others (see column 29, lines 38-43). Thus, it would have been obvious to one skilled in the art at the time the invention was made to have coupled the therapeutic and

diagnostic agents taught by Thorpe et al to the 97A6 monoclonal antibody as taught by Buhring et al [a] for tumor therapy.

Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references.

16. Claims 4-7, 9-10, 12-13 and 78-83 are rejected under 35 U.S.C. 103(a) as being unpatentable over Buhring et al [b] (Blood 94(7):2343-2356, 1 October 1999) as evidenced by Buhring et al [a] (Blood 97(10):3303-3305, 15 May 2001) and as evidenced by Hua et al (Genomics 45(2):412-415, 1997) in view of Thorpe et al (U.S. Patent 6,342,219 B1, filed 4/28/2000).

The claims have been described supra.

Buhring et al [b] as evidenced by Buhring et al [a] and as evidenced by Hua et al have been described supra. Buhring et al [b] does not specifically teach a Fab, F(ab)2, Fv, scFv (interpretation of sFv), a human, a humanized or a chimeric antibody or cytotoxic agents, radioactive isotopes, chemotherapeutic agents and toxins as agents for labeling the antibody. These deficiencies are made up for in the teachings of Thorpe et al.

Thorpe et al have been described supra.

It would have been prima facie obvious to one of ordinary skill in the art at the time the claimed invention was made to have coupled the therapeutic and diagnostic agents taught by Thorpe et al to the 97A6 monoclonal antibody as taught by Buhring et al [b] for tumor therapy.

One of ordinary skill in the art would have been motivated to and had a reasonable expectation of success at the time the invention was made to have coupled the therapeutic and diagnostic agents taught by Thorpe et al to the 97A6 monoclonal antibody as taught by Buhring et al [b] for tumor therapy because Buhring et al [b] teach monoclonal antibody 97A6 and as evidenced by Buhring et al [a] monoclonal antibody 97A6 specifically binds E-NPP3 also known as PDNP3 or PD-1β, which is identical to the protein of SEQ ID NO:743 as evidenced by Hua et al (see the alignment attached to the back of this office action) and Thorpe et al teach immunoconjugates and immunotoxins for tumor therapy, wherein the antibody is a Fab, Fv, single-chain Fv, a human or humanized antibody and the antibody is coupled to toxins that are plant, fungus, or bacterial derived toxins (see column 29, lines 1-18) or coupled to radioactive isotopes (see column 39, lines 31-44) or coupled to chemotherapeutic agents such as taxol, vinblastine, vincristine, colchicines as well as others (see column 29, lines 38-43). Thus, it would have been obvious to one skilled in the art at the time the invention was made to have coupled the therapeutic and diagnostic agents taught by Thorpe et al to the 97A6 monoclonal antibody as taught by Buhring et al [b] for tumor therapy.

Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references.

17. Claims 4-7, 9-10, 12-13 and 78-83 are rejected under 35 U.S.C. 103(a) as being unpatentable over Buhring H-J [c] (U.S. Patent 6,323,321 B1, filed 6/30/1999) as evidenced by Buhring et al [a] (Blood 97(10):3303-3305, 15 May 2001) and as

evidenced by Hua et al (Genomics 45(2):412-415, 1997) in view of Thorpe et al (U.S. Patent 6,342,219 B1, filed 4/28/2000).

The claims have been described supra.

Buhring H-J [c] as evidenced by Buhring et al [a] and as evidenced by Hua et al have been described supra. Buhring H-J [c] does not specifically teach a Fab, F(ab)2, Fv, scFv (interpretation of sFv), a human, a humanized or a chimeric antibody or cytotoxic agents, radioactive isotopes, chemotherapeutic agents and toxins as agents for labeling the antibody. These deficiencies are made up for in the teachings of Thorpe et al.

Thorpe et al have been described supra.

It would have been prima facie obvious to one of ordinary skill in the art at the time the claimed invention was made to have coupled the therapeutic and diagnostic agents taught by Thorpe et al to the 97A6 monoclonal antibody as taught by Buhring H-J [c] for tumor therapy.

One of ordinary skill in the art would have been motivated to and had a reasonable expectation of success at the time the invention was made to have coupled the therapeutic and diagnostic agents taught by Thorpe et al to the 97A6 monoclonal antibody as taught by Buhring H-J [c] for tumor therapy because Buhring H-J [c] teach monoclonal antibody 97A6 and as evidenced by Buhring et al [a] monoclonal antibody 97A6 specifically binds E-NPP3 also known as PDNP3 or PD-1β, which is identical to the protein of SEQ ID NO:743 as evidenced by Hua et al (see the alignment attached to the back of this office action) and Thorpe et al teach immunoconjugates and

immunotoxins for tumor therapy, wherein the antibody is a Fab, Fv, single-chain Fv, a human or humanized antibody and the antibody is coupled to toxins that are plant, fungus, or bacterial derived toxins (see column 29, lines 1-18) or coupled to radioactive isotopes (see column 39, lines 31-44) or coupled to chemotherapeutic agents such as taxol, vinblastine, vincristine, colchicines as well as others (see column 29, lines 38-43). Thus, it would have been obvious to one skilled in the art at the time the invention was made to have coupled the therapeutic and diagnostic agents taught by Thorpe et al to the 97A6 monoclonal antibody as taught by Buhring H-J [c] for tumor therapy.

Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references.

Conclusion

18. No claim is allowed.

19. Any inquiry concerning this communication or earlier communications from the examiner should be directed to David J. Blanchard whose telephone number is (571) 272-0827. The examiner can normally be reached at Monday through Friday from 8:00 AM to 6:00 PM, with alternate Fridays off. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Siew, can be reached at (571) 272-0787. The official fax number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Respectfully,
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